63. (New) The host vector system of Claim 62, wherein said suitable host is a bacterial cell.

64. (New) The host vector system of Claim 62, wherein said suitable host is a eukaryotic cell.

65. (New) A method of producing an APEX protein, comprising:

(a) culturing said host-vector system of Claim 62 under suitable conditions so as to produce said APEX protein; and

(b) recovering said APEX protein so produced.

REMARKS

Claims 1-14, 27-41, and 43-65 are pending. Claims 15-26 and 42 have been cancelled. New Claims 53-65 have been added to replace cancelled Claims 15-26 and 42. The reason for this is that the Examiner has objected to Claims 15-26 and 42 as depending from a nonelected invention. Therefore, Claims 15-26 and 42 are replaced with new Claims 53-64 and 65, respectively, which depend only from an elected invention. Thus, Claims 1-5 and 53-65 are presently under examination.

Attached hereto is "Appendix A", entitled "Amended Claims With Markings to Show Changes Made".

For the sake of clarification, Applicants respectfully point out that the Examiner mistakenly indicated in the Office Action Summary that Claims 1-5, 15-26 and 42 were pending. In fact, Claims 1-52 were pending, of which Claims 6-14, 27-41 and 43-52 were withdrawn from consideration. The Examiner correctly indicated that Claims 1-52 were pending on page 2, paragraph 1 of the Office Action ("Detailed Action").

Restriction:

Applicants' acknowledge the Examiner's comment on page 2, paragraph II, of the Office Action that Claim 43 was inadvertently included in elected Group I, but belongs to nonelected Groups IV-VI, and is therefore withdrawn from consideration as directed to a nonelected invention. Applicants reserve the right to prosecute the subject matter of Claim 43 in one or more continuing applications.

Claim Objections:

The Examiner has objected to Claims 15-26 and 42 because they are dependent on non-elected Claims 6 and 11. As indicated above, Claims 15-26 and 42 have been cancelled and replaced with new Claims 53-64 and 65, respectively, which depend either directly or indirectly from Claim 1, which is directed to an elected invention. Accordingly, Applicants respectfully submit that these claim objections are obviated.

Information Disclosure Statement

The Examiner indicates that Applicants' IDS, filed March 26, 2001 is acknowledged. However, the Examiner states that PTO-1449 form and the references cannot be found. Accordingly, Applicants will resubmit the form PTO-1449 and the references. As the IDS and Supplemental IDS filed in this case are substantial in volume and were originally filed by a representative of Applicants who is no longer prosecuting the present application, Applicants' present representatives are reconstructing these documents and will resubmit them as soon as possible.

Section 112, Second Paragraph, Rejections (Definiteness):

The Examiner has rejected Claims 16 and 21-22 (Claims 16 and 21-22 correspond to new Claims 54 and 59-60, respectively) under 35 U.S.C. 112, second paragraph, as being indefinite.

With respect to Claim 16, the Examiner alleges that "hybridizes under stringent conditions" is ambiguous. This rejection is respectfully traversed.

The Examiner alleges that disclosure of "stringent conditions" set forth at pages 31-32 of the instant specification merely sets forth general parameters for calculating such conditions, and that the specification does not set forth the metes and bounds of this definition. Applicants submit that pages 31-32 do not merely set forth general parameters, but rather specific conditions which are readily recognized by those of skill in the art to result in a clearly and readily detectable hybridization signal. For example, as set forth on page 31, lines 5 and 10, stringent salt conditions are desirably less than about 250 mM NaCl and 25 mM sodium citrate and stringent temperature conditions are at least about 42ºC, respectively. It will be apparent to one of skill in the art that the teachings of the present specification set forth those conditions under which clear hybridization signals may be obtained.

The Examiner alleges that Claims 21 and 22 (Claims 21 and 22 correspond to new Claims 59 and 60, respectively) have no antecedent basis in Claim 1. New Claims 59 and 60 incorporate the Examiner's suggestions, and it is therefore respectfully submitted that this rejection is obviated. Applicants appreciate the Examiner's suggestions.

For these reasons, withdrawal of the rejection under Section 112, second paragraph, is appropriate and respectfully requested.

Section 101 Rejections (Utility):

The Examiner has rejected Claims 1-5, 15-26 and 42 (Claims 15-26 and 42 correspond to new Claims 53-64 and 65, respectively) under 35 U.S.C. 101, alleging that the claimed invention is not supported by either a specific and/or substantial asserted utility or a well established utility. The Examiner alleges that the present specification does not disclose a specific and/or substantial use for the claimed subject matter. In particular, the Examiner alleges that the present specification does not disclose the biological role of the claimed protein or its significance. This rejection is respectfully traversed.

The Examiner directs Applicants to the Revised Interim Utility Guidelines, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999. Applicants respectfully point out that the Revised Interim Utility Guidelines have been superceded by the Utility Examination Guidelines (Federal Register, Vol. 66, No. 6, pages 1092-1099, Friday, January 5, 2001).

In order to satisfy Section 101, the specification must set forth a (1) specific, (2) substantial and (3) credible utility for the claimed invention. The present invention is directed to nucleic acid molecules encoding APEX-1, polynucleotides having certain sequence identity to such nucleic acid molecules, polynucleotides which hybridize to the complement of such nucleic acid molecules, nucleic acid molecules encoding APEX-1 which are labeled with a detectable marker, vectors comprising nucleic acid molecules encoding APEX-1, and host vector systems comprising such vectors.

As set forth in the Utility Examination Guidelines, if the Applicants have asserted that the claimed invention is useful for any particular practical purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, the utility requirement of Section 101 is satisfied. The present specification clearly sets forth both specific and substantial utility for the claimed invention. For example, as pointed out by the Examiner, APEX or an agonist thereof may be administered to treat any number of known disorders, including inflammatory, cancer and immune disorders. It is well established that nucleic acids and proteins encoded thereby, such as APEX, which are shown to be expressed in various tissues, may be biological targets for the treatment of disease states associated with such tissues. Indeed, the patent literature is replete with such examples.

Furthermore, with respect to the credible utility requirement, the present specification states repeatedly that the claimed invention shows homology to a well-characterized class, namely the CD2 subfamily. The Examiner states that the instant situation is directly analogous to that which was addressed in Brenner v. Manson 148, USPQ 689 (1966) (hereinafter "Brenner"). Applicants disagree and respectfully submit that the Examiner's reliance on Brenner is misplaced. Brenner stands for the proposition that a claimed invention must have a practical utility (e.g., must not be

useful solely for research purposes) and that utility is not satisfied merely by showing that a compound yielded belongs to a class of compounds which scientists are screening for possible uses. The present invention does not present such a situation. Rather, the present invention is homologous to the CD2 subfamily, which is well-characterized as having utility with respect to leukocyte proliferation, differentiation, migration and activation, and diseases associated therewith (see, for example, "Background of the Invention" of the present application).

The Examiner further alleges lack of utility by citing various references which purport to teach that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate. However, this is not the standard under the Utility Examination Guidelines or the law. It is established law that when a patent application claiming a nucleic acid asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the Examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such an assertion. "[A] 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient." Fujikawa v. Wattanasin, 93 F.3d 1559, 1565, 39 USPQ2d 1895, 1900 (Fed. Cir. 1996).

Further, the Examiner argues that the function of certain members of the CD2 subfamily have not been elucidated (namely CD84 and Ly9) while SLAM has been shown to enhance antigen-specific proliferation and cytokine production by CD+ T cells, and that it is not clear if APEX of the present application would have such functionality. However, Applicants are not required to show that APEX exhibits functionality to numerous members of a subfamily of which every member is functionally characterized, but rather the Utility Examination Guidelines require that Applicants need only provide one credible assertion of specific and substantial utility to satisfy the utility requirement. The Examiner's position appears to be that the biological functionality of APEX must be proven before utility is established, however that is simply not the law nor is it the standard set forth by the Patent Office.

For these reasons, withdrawal of the rejection under Section 101 is appropriate and respectfully requested.

Section 112, First Paragraph, Rejections (Enablement):

The Examiner has rejected Claims 1-5, 15-26 and 42 (Claims 15-26 and 42 correspond to new Claims 53-64 and 65, respectively) under 35 U.S.C. 112, first paragraph, as not enabling one of skill in the art to make or use the present invention. The Examiner's arguments are the same as those set forth in the Section 101 utility rejection, in that one of skill in the art would not be able to make or use an invention that the Examiner alleges lacks utility, without undue experimentation. The Examiner further alleges that the specification fails to enable a skilled artisan to make the invention commensurate in scope with these claims. This rejection is respectfully traversed.

Applicants reiterate the arguments presented above as to why the present invention satisfies the utility requirement of Section 101, and submit that the present specification teaches the manner in which to make and use the present invention consistent with that utility. For example, one of skill in the art is capable of screening against APEX, using art-recognized assay techniques, to identify modulators thereof, which may be therapeutically useful for the treatment of related disease states.

The Examiner further argues that the sequences provided for APEX-1 (SEQ ID NOS. 1 and 4) fail to make any isolated nucleic acid molecule encoding APEX-1 of Claim 1. However, APEX-1 is described in the present specification as a protein encoded by and having the stated sequences. Therefore, Applicants are unclear as to why the Examiner does not believe a claim directed to APEX-1 is enabled.

With respect to the claims directed to variants and polynucleotides which hybridize to complements of APEX-1, Applicants respectfully submit that one of skill in the art, using the extensive teachings in the present specification, would be able to identify such molecules using art-recognized techniques, commensurate with the utility set forth for APEX-1.

For these reasons, withdrawal of the rejection under Section 112, first paragraph, is appropriate and respectfully requested.

Section 112, First Paragraph, Rejections (Written Description):

The Examiner has rejected Claims 1-5, 15-26 and 42 (Claims 15-26 and 42 correspond to new Claims 53-64 and 65, respectively) under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is respectfully traversed.

As stated above, the present specification describes APEX-1 has a molecule having the amino acid sequence set forth in SEQ ID NO:4 and encoded by a nucleic acid having the sequence set forth in SEQ ID NO:1. Therefore, Applicants are unclear as to why the Examiner believes that the present specification does not provide adequate written description for APEX-1. With respect to the claims directed to variants and polynucleotides which hybridize to complements of APEX-1, Applicants respectfully submit that one of skill in the art, using the extensive teachings in the present specification, would recognize Applicants to be in possession of such molecules. Such molecules are recognized as having the utility set forth with respect for APEX-1, and one of skill in the art will be capable of using the sequences set forth in the present specification to identify variations thereof which are within the scope of the present invention.

For these reasons, withdrawal of the rejection under Section 112, first paragraph, is appropriate and respectfully requested.

Section 102 Rejections:

The Examiner has rejected Claims 1, 3-5 and 15-19 (Claims 15-19 correspond to new Claims 53-57, respectively) under 35 U.S.C. 102(a) as being anticipated by PCT publication WO 99/6308. Applicants assume that this is a typographical error and that the Examiner means to refer to PCT publication WO 99/63088 ("the '088 publication"), as that is the reference that was mailed

with the Office Action. The Examiner alleges that the '088 publication teaches a 1,076 isolated nucleic acid sequence encoding MP-7 which has the amino acid sequence shown in the instant claimed SEQ ID NO:4.

Applicants submit herewith a Declaration of Prior Invention in the United States to Overcome a Reference Under 37 C.F.R. 1.131 (hereinafter "Rule 131 Declaration"), establishing a date of invention prior to the publication date of the '088 publication. As the inventors are no longer employed by the assignee to the present application, Applicants' representative has been unable to obtain signatures prior to the present submission. Applicants' representative is in the process of obtain the inventors' signatures and a fully executed Rule 131 Declaration will be submitted as soon as possible. In view of this Rule 131 Declaration, Applicants submit that the '088 publication is not prior art to the present invention, and therefore respectfully submit that the rejection under Section 102(a) is obviated.

The Examiner has rejected Claims 15-17 (Claims 15-17 correspond to new Claims 53-55, respectively) under 35 U.S.C. 102(b) as being anticipated by Hillier et al. (GenBank Accession No. H73135) ("Hillier"). The Examiner alleges that Hillier teaches a 436 polynucleotide having 100% polynucleotide identity to the polynucleotide at positions 49-306 of the claimed SEQ ID NO:1. This rejection is respectfully traversed.

It is well-established that in order for a reference to serve as prior art, it must demonstrate that the claimed invention was in the possession of the public as dictated by the patent statute or case law, including containing a sufficient description of, and an enabling disclosure for, the claimed invention. The reference must contain sufficient technical information to describe the claimed invention to a person of ordinary skill in the art to which the claimed invention pertains and to enable such a person to make and use the claimed subject matter, without requiring undue experimentation.

Claims 53-55 are directed to polynucleotides having at least 70% identity to a polynucleotide encoding APEX-1, polynucleotides which hybridize under stringent conditions to the complement of a polynucleotide encoding APEX-1 and isolated nucleic acid molecules comprising a nucleotide

sequence which is complementary to a polynucleotide encoding APEX-1. Hillier merely sets forth an Expressed Sequence Tag which fails to contain a written description or enabling disclosure of any such polynucleotides or nucleic acid molecules. Regardless of any sequence identity between the sequence of Hillier and SEQ ID NO:1, there is no teaching in Hillier which provides the requisite technical information to describe the claimed invention to a person of ordinary skill in the art. Accordingly, withdrawal of the rejection under Section 102(b) is appropriate and respectfully requested.

The Examiner has rejected Claims 1, 18 and 20 (Claims 18 and 20 correspond to new Claims 56 and 58, respectively) under 35 U.S.C. 103(a) as being unpatentable over the '088 publication in view of Adams et al. (Biochemistry of the Nucleic Acids). For the reasons set forth above, the '088 publication is not prior art to the present invention. Accordingly, Applicants respectfully submit that this rejection is obviated.

The Examiner has rejected Claims 21-22 (Claims 21-22 correspond to new Claims 59-60, respectively) under 35 U.S.C. 103(a) as being unpatentable over the '088 publication in view of U.S. Patent No. 6,134,002. For the reasons set forth above, the '088 publication is not prior art to the present invention. Accordingly, Applicants respectfully submit that this rejection is obviated.

The Examiner has rejected Claims 23-26 and 42 (Claims 23-26 and 42 correspond to new Claims 61-64 and 65, respectively) under 35 U.S.C. 103(a) as being unpatentable over the '088 publication in view of Darnell et al. For the reasons set forth above, the '088 publication is not prior art to the present invention. Accordingly, Applicants respectfully submit that this rejection is obviated.

The Examiner has indicated that formal drawings have been submitted which fail to comply with 37 C.F.R. 1.84. A new set of formal drawings will be submitted.

The Examiner statement that the nucleotide sequence of SEQ ID NO:1 is free of prior art is acknowledged.

Please direct any questions concerning this Response or any aspect of this case to the undersigned attorney.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Account No. 19-3880 in the name of Bristol-Myers Squibb Company.

Respectfully submitted,

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Date: December 4, 2002

Appendix A

AMENDED CLAIMS WITH MARKINGS TO SHOW CHANGES MADE

53. (New) An isolated polynucleotide variant having at least 70% polynucleotide sequence identity to said isolated nucleic acid molecule of Claim 1.

54. (New) An isolated polynucleotide which hybridizes under stringent conditions to the complement of said isolated nucleic acid molecule of Claim 1.

55. (New) An isolated nucleic acid comprising a nucleotide sequence which is complementary to said isolated nucleic acid molecule of Claim 1.

56. (New) The isolated nucleic acid molecule of Claim 1 which is DNA or RNA.

57. (New) The isolated nucleic acid molecule of Claim 56, wherein said DNA is cDNA.

58. (New) The isolated nucleic acid molecule of Claim 56, wherein said RNA is mRNA.

59. (New) A labeled nucleic acid molecule, wherein said isolated nucleic acid molecule of Claim 1 is labeled with a detectable marker.

60. (New) The labeled nucleic acid molecule of Claim 59, wherein said detectable marker is selected from the group consisting of a radioisotope, a fluorescent compound, a bioluminescent compound, a chemiluminescent compound, a metal chelator and an enzyme.

61. (New) A vector comprising said isolated nucleic acid molecule of Claim 1.

62. (New) A host vector system comprising said vector of Claim 61 in a suitable host cell.

63. (New) The host vector system of Claim 62, wherein said suitable host is a bacterial cell.

64. (New) The host vector system of Claim 62, wherein said suitable host is a eukaryotic cell.

65. (New) A method of producing an APEX protein, comprising:

(a) culturing said host-vector system of Claim 62 under suitable conditions so as to produce said APEX protein; and

(b) recovering said APEX protein so produced.